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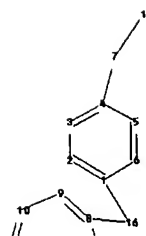
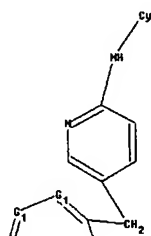
* * * * * Welcome to STN International * * * * *
* * * * * STN Columbus * * * * *

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=> Uploading C:\Program Files\Stnexp\Queries\Queries\amended10766181.str



chain nodes :

7 16 17

ring nodes :

1 2 3 4 5 6 8 9 10 11 12 13

chain bonds :

1-16 4-7 7-17 8-16

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 8-13 8-9 9-10 10-11 11-12 12-13

exact/norm bonds :

1-16 4-7 7-17 8-13 8-9 8-16 9-10 10-11 11-12 12-13

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1-2 1-6 2-3 3-4 4-5 5-6

G1:C,N

Match level :

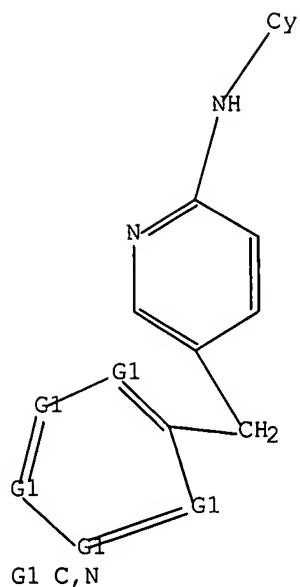
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:Atom 9:Atom 10:CLASS  
11:CLASS 12:CLASS 13:CLASS 16:CLASS 17:Atom

L1 STRUCTURE UPLOADED

=> dis l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 sam

L2 8 SEA SSS SAM L1

=> s l1 full

L3 110 SEA SSS FUL L1

=> file caplus

=> s l3

L4 12 L3

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20730665 PD<FEB 2000

(PD<20000200)

L5 1 L4 AND PD<FEB 2000

=> dis l5 bib abs hitstr

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1998:545594 CAPLUS Full-text

DN 129:148914

TI Preparation of 2-amino-4-aryl-5-arylmethyl-5-cyclopentyl-3-hydroxymethylpyridines and related compounds for treatment of arteriosclerosis.

IN Schmeck, Carsten; Brandes, Arndt; Loegers, Michael; Schmidt, Gunter; Bremm, Klaus-Dieter; Bischoff, Hilmar; Schmidt, Delf; Schuhmacher, Joachim

PA Bayer A.-G., Germany

SO Ger. Offen., 22 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

PATENT NO.

KIND

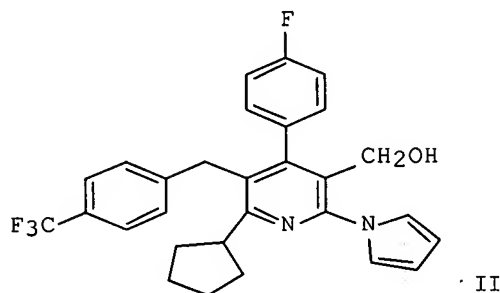
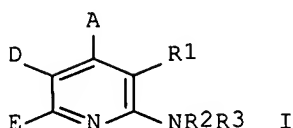
DATE

APPLICATION NO.

DATE

## 10/766,181 (amended)

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 CA 2279636 A1 19980813 CA 1998-2279636 19980123 <--  
 WO 9834920 A1 19980813 WO 1998-EP362 19980123 <--  
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 KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,  
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 UA, UG, US, UZ, VN, YU, ZW  
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 GA, GN, ML, MR, NE, SN, TD, TG  
 AU 9862123 A 19980826 AU 1998-62123 19980123 <--  
 AU 730109 B2 20010222  
 BR 9807181 A 20000125 BR 1998-7181 19980123 <--  
 EP 973744 A1 20000126 EP 1998-904126 19980123 <--  
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 HU 200001022 A2 20000928 HU 2000-1022 19980123  
 NZ 337011 A 20010427 NZ 1998-337011 19980123  
 JP 2001510478 T 20010731 JP 1998-533691 19980123  
 NO 9903738 A 19990917 NO 1999-3738 19990802 <--  
 BG 103631 A 20001130 BG 1999-103631 19990803  
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 OS MARPAT 129:148914  
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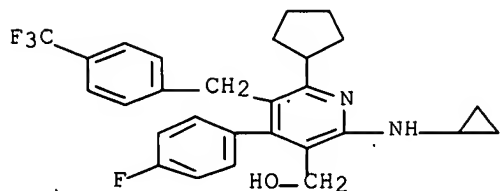


AB Title compds. [I; A = (substituted) aryl; D = (substituted) aryl, R6L, etc.; R6 = (substituted) cycloalkyl, aryl, (benzocondensed) mono-, di-, or tricyclic heterocyclyl; L = (substituted) alkyl, alkenyl; E = cycloalkyl, (substituted) alkyl; R1 = hydroxyalkyl; R2, R3 = H, Ph, PhCH2, cycloalkyl, alkyl, acyl, aminocarbonyl; R2R3N = 5-7 membered (unsatd.) (benzocondensed) (substituted) heterocyclyl], were prepared Thus, title compound (II) inhibited cholesteryl ester transfer protein with IC50 = 6 + 10-8 M.

IT 210981-29-6P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of 2-amino-4-aryl-5-arylmethyl-5-cyclopentyl-3-hydroxymethylpyridines and related compds. for treatment of arteriosclerosis)

RN 210981-29-6 CAPLUS  
 CN 3-Pyridinemethanol, 6-cyclopentyl-2-(cyclopropylamino)-4-(4-fluorophenyl)-

5-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



=&gt; s 14 not 15

L6 11 L4 NOT L5

=&gt; dis 16 1-11 bib abs fhitr

L6 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:510469 CAPLUS Full-text

DN 146:501037

TI Preparation of pyridine derivatives and analogs thereof as glucokinase activators

IN Aicher, Thomas Daniel; Lee, Wai-Man; Hinklin, Ronald Jay; Chicarelli, Mark Joseph; Boyd, Steven Armen; Condroski, Kevin Ronald

PA Array Biopharma Inc., USA

SO PCT Int. Appl., 190pp.

CODEN: PIXXD2

DT Patent

LA English

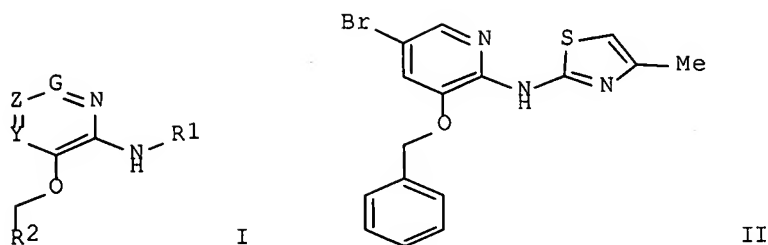
FAN.CNT 1

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PRAI US 2005-732037P P 20051101

OS MARPAT 146:501037

GI



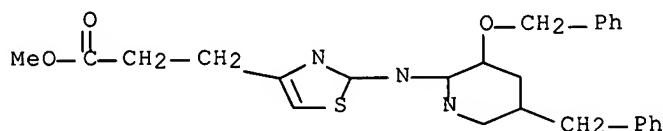
AB Title compds. I [R1 = (un)substituted heteroaryl; R2 = (un)substituted monocyclic aryl, bicyclic aryl or heteroaryl; Z = N or CR3, wherein R3 = H, (un)substituted alkyl, alkenyl, etc.; Y = N or CR4, wherein R4 = H, Me, Et, etc.; G = N or CR5, wherein R5 = H, Me, Et, etc.; at least one of G or Z is not N], and their pharmaceutically acceptable salts, are prepared and disclosed as glucokinase activators. Thus, e.g., II·HCl was prepared via bromination of 3-(benzyloxy)pyridin-2-amine followed by condensation with benzoyl isothiocyanate to generate 1-benzoyl-3-[3-(benzyloxy)-5-bromopyridin-2-yl]thiourea intermediate which undergoes hydrolysis and heterocyclization with 1-chloropropan-2-one. The glucokinase activity of certain compds. of the invention was evaluated in glucose S0.5 assay with S0.5 values ranging from 1.5 to 4.0 mM.

IT 936246-39-8P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of pyridine derivs. and analogs thereof as glucokinase activators)

RN 936246-39-8 CAPLUS

CN 4-Thiazolepropanoic acid, 2-[[3-(phenylmethoxy)-5-(phenylmethyl)-2-pyridinyl]amino]-, methyl ester, hydrochloride (1:1) (CA INDEX NAME)



● HCl

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:886963 CAPLUS Full-text

DN 145:299522

TI Pharmaceutical combination of Bcr-Abl and RAF inhibitors

IN Manley, Paul W.

PA Novartis AG, Switz.; Novartis Pharma GmbH

SO PCT Int. Appl., 31pp.

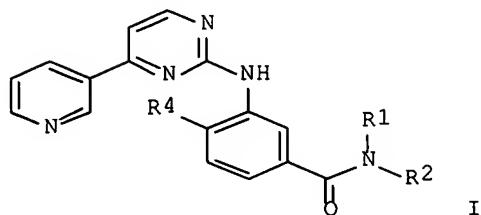
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006089781	A1	20060831	WO 2006-EP1740	20060224
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PRAI	US 2005-656340P	P	20050225		
OS	MARPAT 145:299522				
GI					



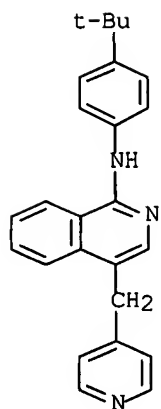
AB The invention provides a pharmaceutical combination comprising: (a) a pyrimidinylaminobenzamide compound, and (b) a RAF kinase inhibitor and a method for treating or preventing a proliferative disease using such a combination, wherein compound (a) has the following general Formula: (I), with R1, R2, and R4 defined in claims.

IT 258851-00-2

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (pharmaceutical combination of Bcr-Abl and RAF inhibitors)

RN 258851-00-2 CAPLUS

CN 1-Isoquinolinamine, N-[4-(1,1-dimethylethyl)phenyl]-4-(4-pyridinylmethyl)-  
 (9CI) (CA INDEX NAME)



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 2006:513675 CAPLUS Full-text  
DN 145:34151  
TI Combinations of JAK kinase inhibitors  
IN Cooke, Nigel Graham; Manley, Paul W.  
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.  
SO PCT Int. Appl., 61 pp.  
CODEN: PIXXD2

DT Patent  
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006056399	A2	20060601	WO 2005-EP12480	20051122
	WO 2006056399	A3	20060831		
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	AU 2005309019	A1	20060601	AU 2005-309019	20051122
PRAI	US 2004-630713P	P	20041124		
	WO 2005-EP12480	W	20051122		

AB The invention provides a pharmaceutical combination comprising (a) at least one agent selected from Bcr-Abl, Flt-3, FAK and RAF kinase inhibitors; and (b) at least one JAK kinase inhibitor, and a method for treating or preventing a proliferative disease using such a combination. A preferred embodiment of the invention is the combination of a RAF inhibitor, e.g., (4-tert-butylphenyl)-(4-pyridin-4-yl-methyl-isoquinolin-1-yl)amine or [4,7']bi-isoquinolinyl-1-yl-4-(tert-butylphenyl)amine, and a JAK kinase inhibitor, such as PNU 156804 or WHI-P 131 for the treatment of myelomas, especially multiple myeloma.

IT 258851-00-2

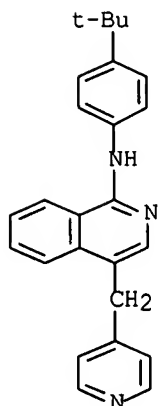
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

## 10/766,181 (amended)

(combinations of JAK kinase inhibitors with other protein kinase inhibitors for treatment or prevention of proliferative disease)

RN 258851-00-2 CAPLUS

CN 1-Isoquinolinamine, N-[4-(1,1-dimethylethyl)phenyl]-4-(4-pyridinylmethyl)-  
(9CI) (CA INDEX NAME)



L6 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:878558 CAPLUS Full-text

DN 141:360667

TI Methods for treating and diagnosing diseases having an aberrant MAP kinase signaling pathway, such as proliferative diseases, and for monitoring the effectiveness of treatment of proliferative diseases

IN Hu, Ping; Wang, Yingqi Karen; Batt, David Bryant

PA Novartis Ag, Switz.; Novartis Pharma GmbH

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004090545	A2	20041021	WO 2004-EP3877	20040413
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	AU 2004227103	A1	20041021	AU 2004-227103	20040413
	CA 2522333	A1	20041021	CA 2004-2522333	20040413
	EP 1616191	A2	20060118	EP 2004-726981	20040413
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	BR 2004009409	A	20060425	BR 2004-9409	20040413
	CN 1784602	A	20060607	CN 2004-80011895	20040413



## 10/766,181 (amended)

JP 2006525962	T	20061116	JP 2006-505103	20040413
US 2007099250	A1	20070503	US 2005-553091	20051013
IN 2005CN02990	A	20070727	IN 2005-CN2990	20051114
PRAI US 2003-462723P	P	20030414		
WO 2004-EP3877	W	20040413		

AB The present invention relates to phosphoproteins useful as biomarkers for identifying and treating patients suffering from diseases characterized by an aberrant MAP kinase signaling pathway, for example proliferative diseases like certain cancers, monitoring the efficacy of treatment of patients having the disease by administering Raf kinase inhibitors and diagnosing the disease in patients.

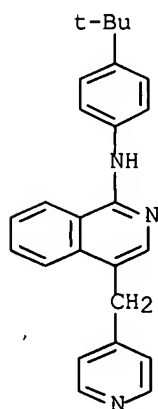
IT 258851-00-2, BPMI

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Raf inhibitor; phosphoproteins as biomarkers in treatment and diagnosis of diseases having aberrant MAP kinase signaling pathway, such as proliferative diseases, and for monitoring treatment effectiveness)

RN 258851-00-2 CAPLUS

CN 1-Isoquinolinamine, N-[4-(1,1-dimethylethyl)phenyl]-4-(4-pyridinylmethyl)-(9CI) (CA INDEX NAME)



L6 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:780541 CAPLUS Full-text

DN 141:295873

TI Preparation of N-aryl (heteroarylalkyl)isoquinolineamines as inhibitors of mutant and wild-type MAP kinases for the treatment of cancer

IN Batt, David Bryant; Bold, Guido; Kim, Sunkyu; Ramsey, Timothy Michael; Sabio, Michael Lloyd

PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.

SO PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

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## 10/766,181 (amended)

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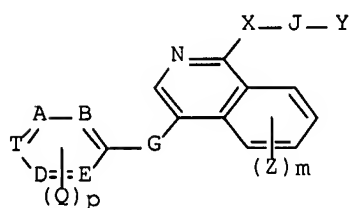
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CA 2518530	A1	20040923	CA 2004-2518530	20040310
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
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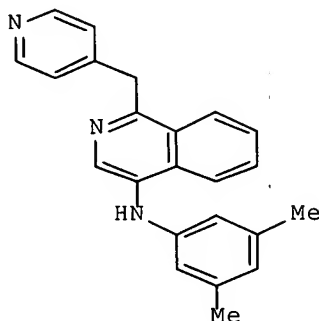
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JP 2006519807	T	20060831	JP 2006-504625	20040310
ZA 2005006571	A	20060726	ZA 2005-6571	20050817
NO 2005004647	A	20051209	NO 2005-4647	20051010

PRAI US 2003-453624P	P	20030311
WO 2004-EP2460	A	20040310

OS MARPAT 141:295873  
 GI



I



II

AB Compds. I [A, B, D, E, T = CH, N (independent; between one and three of A, B, D, E, or T are N); G = alkylene, CH<sub>2</sub>O, CH<sub>2</sub>S, CH<sub>2</sub>NH, SO<sub>2</sub>, O, S, NR; J = (CHR)<sub>n</sub>; R = H, alkyl; X = Y, RN, O, S; Y = H, (un)substituted alkyl, aryl, heteroaryl, cycloalkyl; Z = halogen, hydroxy, nitro, cyano, carboxy, (un)substituted amino, alkoxy, alkylcarbonyloxy, alkoxy carbonyl, etc.; m = 0-4; n, p = 0-2], particularly N-aryl (azaheteroarylalkyl)isoquinolineamines such as II, are prepared as inhibitors of MAP kinases for use in the treatment of cancers; I are especially useful in the treatment of cancers possessing mutant Raf kinases, such as melanoma. 2-(Cyanomethyl)benzoic acid is esterified with DMF di-Me acetal to give its Me ester which undergoes condensation with 4-pyridinecarboxaldehyde followed by reesterification of the benzoic acid to yield 2-(2-methoxycarbonylphenyl)-3-(4-pyridinyl)acrylonitrile (III); hydrogenation and concomitant cyclocondensation of III yields 4-(4-pyridylmethyl)-1-isoquinolinone which is then chlorinated to yield 1-chloro-4-(4-pyridinylmethyl)isoquinoline (IV). Condensation of IV with 3,5-dimethylaniline yields II. Compds. of the invention inhibit either wild-type C-Raf with IC<sub>50</sub> values between 0.01 μM and 3.5 μM, wild-type B-Raf with IC<sub>50</sub> values between 0.03 μM and 3.7 μM, or a mutant B-Raf (V599E) with IC<sub>50</sub> values between 0.01 μM and 3.4 μM (no data).

IT 258850-90-7P

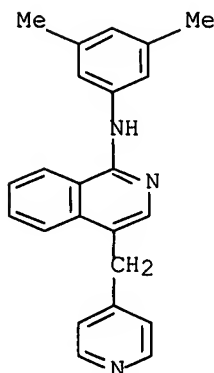
10/766,181 (amended)

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)

(preparation of mutant and wild-type MAP kinase-inhibiting N-aryl  
(heteroarylalkyl)isoquinolineamines as potential anticancer agents)

RN 258850-90-7 CAPLUS

CN 1-Isoquinolinamine, N-(3,5-dimethylphenyl)-4-(4-pyridinylmethyl)- (9CI)  
(CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:113527 CAPLUS Full-text

DN 140:163891

TI Preparation of substituted pyridines and pyridazines with angiogenesis  
inhibiting activity for pharmaceutical use as antitumor agents

IN Dumas, Jacques P.; Boyer, Stephen James; Dixon, Julie A.; Joe, Teddy Kite;  
Kluender, Harold C. E.; Lee, Wendy; Nagarathnam, Dhanapalan; Sibley,  
Robert N.; Su, Ning

PA Bayer Pharmaceuticals Corporation, USA

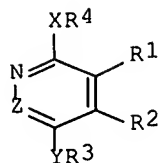
SO U.S., 60 pp.  
CODEN: USXXAM

DT Patent

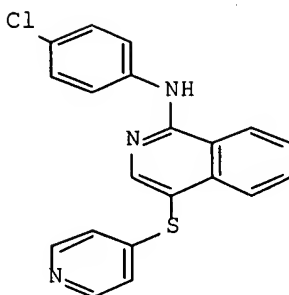
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	US 6689883	B1	20040210	US 2000-672294	20000928
	US 2004092740	A1	20040513	US 2003-720702	20031124
PRAI	US 1999-287595P	P	19990928		
	US 2000-672294	A3	20000927		
OS	MARPAT 140:163891				
GI					



I



II

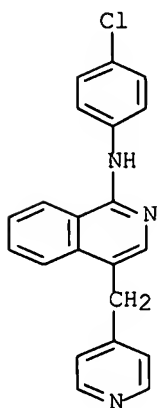
AB Fused ring systems with a pyridine or pyridazine subunit, such as I [X = connecting group, such as O, S, NH, etc.; Y = connecting group, such as O, S, CH<sub>2</sub>O, CH<sub>2</sub>S, NH, OCH<sub>2</sub>, SCH<sub>2</sub>, SO, SO<sub>2</sub>, etc.; Z = CH, N; R<sub>1</sub>R<sub>2</sub> = fused ring, such as CH:CHCH:CH, CH:CHS, CH:CHO, CH:CHNH, N:CHNH, N:NNH, etc.; R<sub>3</sub>, R<sub>4</sub> = aryl, heteroaryl, etc.; XR<sub>4</sub> = nitrogen bound heterocyclyl, such as 1-indoliny], with angiogenesis inhibiting activity were prepared for pharmaceutical use as antitumor agents. Thus, substituted isoquinoline II was prepared in a 3 step sequence which included bromination of isocarbostyryl to form 1,4-dibromoisquinoline in 96% yield, followed by monoamination with 4-chloroaniline to give 4-bromo-N-(4-chlorophenyl)-1-isoquinolinamine in 64.4% yield, and subsequent reaction with 4-mercaptopyridine to give II in 19% yield. The prepared compds. were tested for KDR receptor inhibition.

IT 258850-91-8P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of substituted pyridines and pyridazines with angiogenesis inhibiting activity for pharmaceutical use as antitumor agents)

RN 258850-91-8 CAPLUS

CN 1-Isoquinolinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RE.CNT 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 2003:570820 CAPLUS Full-text

## 10/766,181 (amended)

DN 139:111640  
 TI Anti-angiogenesis combination therapies using KDR inhibitor pyridazine or pyridine derivatives  
 IN Adams, Paul E.; Boyer, Stephen J.; Dumas, Jacques; Elting, James J.; Kluender, Harold C. E.  
 PA Bayer Corporation, USA; Bayer Pharmaceuticals Corporation  
 SO PCT Int. Appl., 127 pp.  
 CODEN: PIXXD2

DT Patent  
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003059354	A2	20030724	WO 2002-US41145	20021220
	WO 2003059354	A3	20031113		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2471314	A1	20030724	CA 2002-2471314	20021220
	AU 2002364102	A1	20030730	AU 2002-364102	20021220
	EP 1467736	A2	20041020	EP 2002-798573	20021220
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	JP 2006503796	T	20060202	JP 2003-559516	20021220
	MX 2004PA05561	A	20041206	MX 2004-PA5561	20040609
	US 2005019424	A1	20050127	US 2004-498935	20040616
PRAI	US 2001-344294P	P	20011221		
	WO 2002-US41145	W	20021220		

OS MARPAT 139:111640

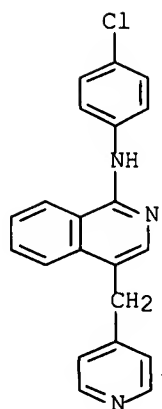
AB The invention discloses the use of substituted fused or unfused pyridazine or pyridine derivs. which are KDR inhibitors in combination with other chemotherapeutic agents for use in treatment of diseases associated with abnormal angiogenesis and/or hyperpermeability and/or hyperproliferative diseases, e.g. cancer.

IT 258850-91-8

RL: PAC (Pharmacological activity); BIOL (Biological study)  
 (anti-angiogenesis combination therapies using KDR inhibitor pyridazine or pyridine derivs.)

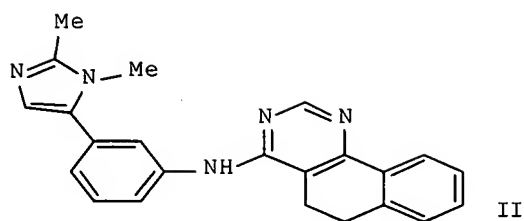
RN 258850-91-8 CAPLUS

CN 1-Isoquinolinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2001:851122 CAPLUS Full-text  
 DN 135:371759  
 TI Preparation of N-imidazolylphenyl-5,6-dihydrobenzo[h]quinazolin-4-amines  
 and other N-containing heterocyclic amines as 5-hydroxytryptamine  
 antagonists for treatment of CNS disorders  
 IN Yamada, Akira; Spears, Glen; Hayashida, Hisashi; Tomishima, Masaki; Ito,  
 Kiyotaka; Imanishi, Masashi  
 PA Fujisawa Pharmaceutical Co., Ltd., Japan  
 SO PCT Int. Appl., 154 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001087845	A2	20011122	WO 2001-JP4002	20010514
	WO 2001087845	A3	20020829		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 2001056728	A5	20011126	AU 2001-56728	20010514
	US 2003176454	A1	20030918	US 2002-258582	20021101
PRAI	AU 2000-7501	A	20000515		
	AU 2000-1955	A	20001207		
	WO 2001-JP4002	W	20010514		
OS	MARPAT 135:371759				
GI					



AB Title compds. AMQNHZ [I; wherein A = H, (un)substituted, unsatd., N-containing heterocyclic group, or C(NH)NHR; R = (un)substituted aryl or heterocyclic group; M = (CH<sub>2</sub>)<sub>n</sub>, (CH<sub>2</sub>)<sub>n</sub>O(CH<sub>2</sub>)<sub>m</sub>, or (CH<sub>2</sub>)<sub>n</sub>NH(CH<sub>2</sub>)<sub>m</sub>; n and m = independently 0-2; Q = (un)substituted cycloalkylene group, arylene, or divalent heterocyclic group; Z = (un)substituted, unsatd., mono-, di-, tri-, or tetra-cyclic, N-containing heterocyclic group which may contain addnl. N, O, and S atoms as the ring member(s), e.g. indeno[1,2,3- de]phthalazinyl or 5,6-dihydrobenzo[h]quinazolinyl; and the prodrugs or pharmaceutically acceptable salts thereof] were prepared. For example, a mixture of 4-chloro-5,6-dihydrobenzo[h]quinazoline, 3-(1,2-dimethyl-1H-imidazol-5-yl)aniline, and 1,3-dimethyl-2-imidazolidinone was heated for an hour at 200°C, cooled, treated with 1N aqueous NaOH and water, and worked up to give II. I are 5-hydroxytryptamine (5-HT) antagonists useful for the prevention and/or treatment of central nervous system (CNS) disorders, such as anxiety, depression, obsessive compulsive disorders, migraine, anorexia, Alzheimer's disease, sleep disorders, bulimia, panic attacks, withdrawal from drug abuse, schizophrenia, and disorders associated with spinal trauma and/or head injury (no data).

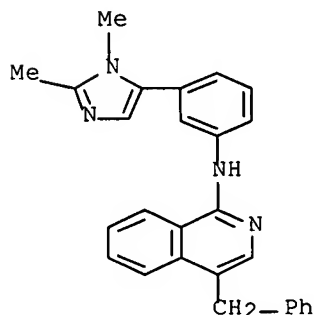
IT 374556-53-3P, 4-Benzyl-N-[3-(1,2-dimethyl-1H-imidazol-5-yl)phenyl]-1-isoquinolinamine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-(imidazolylphenyl)dihydrobenzo[h]quinazolinamines and other N-containing heterocyclic amines as 5-hydroxytryptamine antagonists for treatment of CNS disorders)

RN 374556-53-3 CAPLUS

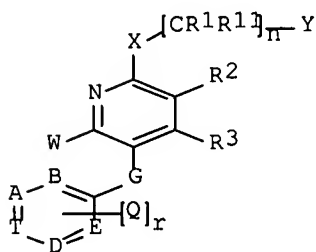
CN 1-Isoquinolinamine, N-[3-(1,2-dimethyl-1H-imidazol-5-yl)phenyl]-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



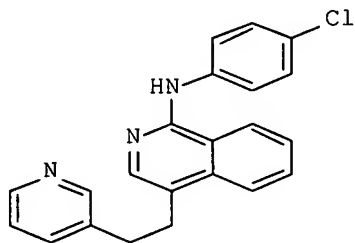
L6 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN  
 AN 2001:597986 CAPLUS Full-text  
 DN 135:180710

TI Preparation of isoquinolinamines inhibiting angiogenesis and/or VEGF  
receptor tyrosine kinase  
IN Bold, Guido; Manley, Paul William  
PA Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft  
m.b.H.  
SO PCT Int. Appl., 98 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001058899	A1	20010816	WO 2001-EP1331	20010207
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001031710	A5	20010820	AU 2001-31710	20010207
	EP 1254138	A1	20021106	EP 2001-903716	20010207
	EP 1254138	B1	20050511		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003522773	T	20030729	JP 2001-558449	20010207
	AT 295365	T	20050515	AT 2001-903716	20010207
	PT 1254138	T	20050930	PT 2001-903716	20010207
	ES 2241781	T3	20051101	ES 2001-1903716	20010207
	US 2003158409	A1	20030821	US 2002-203579	20021011
	US 6706731	B2	20040316		
	HK 1052500	A1	20060224	HK 2003-103231	20030506
	US 2004209894	A1	20041021	US 2004-766181	20040127
PRAI	CH 2000-265	A	20000209		
	WO 2001-EP1331	W	20010207		
	US 2002-203579	A1	20021011		
OS	MARPAT 135:180710				
GI					



I



II

AB The title compds. [I; A, D, T = N, CH, CR4 (with the proviso that at least one of A and D = CR4 when T = N); R4 = alkyl, alkenyl, alkylthio, etc.; B, E = N, CH; G = alkylene, alkenylene, CH2OCH2, etc.; n = 0-2; Q = alkyl, whereby A, D and T are not substituted by Q if they represent CR4; r = 0-5; R1, R11 = H, alkyl; R2, R3 = alkyl; or R2 and R3 together form a bridge to form



10/766,181 (amended)

isoquinoline, naphthyridine, etc.; X = NR<sup>5</sup>, O, S; R<sup>5</sup> = H, alkyl; Y = H, aryl, heterocyclyl, etc.], useful for the treatment of a disease which responds to an inhibition of angiogenesis, were prepared and formulated. E.g., a multi-step synthesis of II which showed IC<sub>50</sub> of 0.105  $\mu$ M against KDR VEGF-receptor tyrosine kinase, was given.

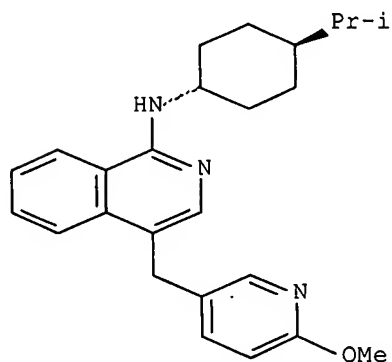
IT 355013-23-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of isoquinolinamines inhibiting angiogenesis and/or VEGF receptor tyrosine kinase)

RN 355013-23-9 CAPLUS

CN 1-Isoquinolinamine, 4-[(6-methoxy-3-pyridinyl)methyl]-N-[trans-4-(1-methylethyl)cyclohexyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:247328 CAPLUS Full-text

DN 134:266326

TI Preparation of substituted pyridines and pyridazines with angiogenesis inhibiting activity for pharmaceutical use as antitumor agents

IN Dumas, Jacques P.; Joe, Teddy Kite; Kluender, Harold C. E.; Lee, Wendy; Nagarathnam, Dhanapalan; Sibley, Robert N.; Su, Ning; Boyer, Stephen James; Dixon, Julie A.

PA Bayer Corporation, USA

SO PCT Int. Appl., 120 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

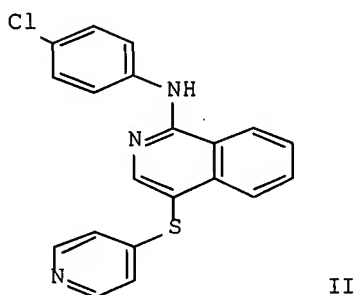
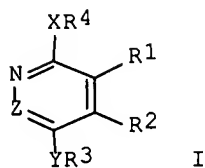
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001023375	A2	20010405	WO 2000-US26500	20000926
	WO 2001023375	A3	20020502		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW

## 10/766,181 (amended)

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

TW 593315	B	20040621	TW 2000-89119700	20000925
CA 2385817	A1	20010405	CA 2000-2385817	20000926
EP 1228063	A2	20020807	EP 2000-978215	20000926
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
HU 200202704	A2	20021228	HU 2002-2704	20000926
BR 2000014382	A	20030624	BR 2000-14382	20000926
EE 200200161	A	20030815	EE 2002-161	20000926
JP 2003526632	T	20030909	JP 2001-526527	20000926
NZ 518589	A	20050324	NZ 2000-518589	20000926
AU 782820	B2	20050901	AU 2001-15696	20000926
RU 2260008	C2	20050910	RU 2002-111414	20000926
CN 1769282	A	20060510	CN 2005-10127109	20000926
CN 1769283	A	20060510	CN 2005-10127110	20000926
NO 2002001520	A	20020523	NO 2002-1520	20020326
MX 2002PA03156	A	20020930	MX 2002-PA3156	20020326
ZA 2002002760	A	20030818	ZA 2002-2760	20020409
IN 2002MN00458	A	20050318	IN 2002-MN458	20020412
BG 106637	A	20030228	BG 2002-106637	20020423
PRAI US 1999-407600	A	19990928		
CN 2000-816369	A3	20000926		
WO 2000-US26500	W	20000926		
OS MARPAT 134:266326				
GI				



AB Fused ring systems with a pyridine or pyridazine subunit, such as I [X = connecting group, such as O, S, NH, etc.; Y = connecting group, such as O, S, CH<sub>2</sub>O, CH<sub>2</sub>S, NH, OCH<sub>2</sub>, SCH<sub>2</sub>, SO, SO<sub>2</sub>, etc.; Z = CH, N; R<sub>1</sub>R<sub>2</sub> = fused ring, such as CH:CHCH:CH, CH:CHS, CH:CHO, CH:CHNH, N:CHNH, N:NNH, etc.; R<sub>3</sub>, R<sub>4</sub> = aryl, heteroaryl, etc.; XR<sub>4</sub> = nitrogen bound heterocyclyl, such as 1-indolinyl], with angiogenesis inhibiting activity were prepared for pharmaceutical use as antitumor agents. Thus, substituted isoquinoline II was prepared in a 3 step sequence which included bromination of isocarbostyryl to form 1,4-dibromoisquinoline in 96% yield, followed by monoamination with 4-chloroaniline to give 4-bromo-N-(4-chlorophenyl)-1- isoquinolinamine in 64.4% yield, and subsequent reaction with 4-mercaptopyridine to give II in 19% yield. The prepared compds. were tested for KDR receptor inhibition.

IT 258850-91-8P

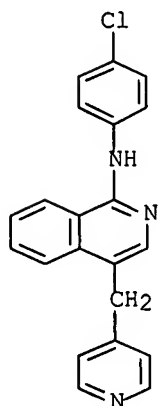
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT

(Reactant or reagent); USES (Uses)

(preparation of substituted pyridines and pyridazines with angiogenesis inhibiting activity for pharmaceutical use as antitumor agents)

RN 258850-91-8 CAPLUS

CN 1-Isoquinolinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2000:133671 CAPLUS Full-text

DN 132:166131

TI Preparation of isoquinolines with angiogenesis inhibiting activity

IN Altmann, Karl-Heinz; Bold, Guido; Manley, Paul William

PA Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H

SO PCT Int. Appl., 74 pp.

CODEN: PIXXD2

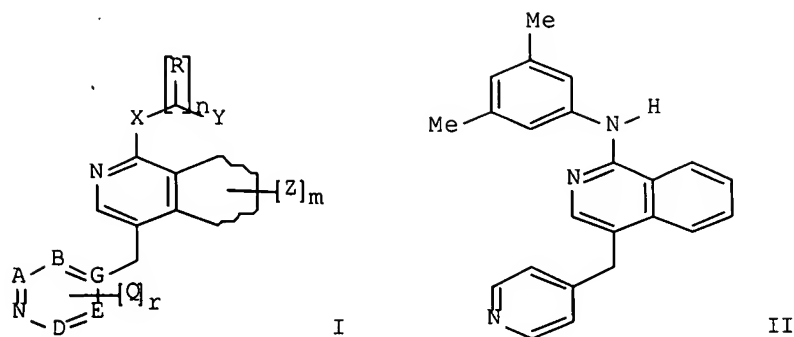
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000009495	A1	20000224	WO 1999-EP5781	19990809
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2339961	A1	20000224	CA 1999-2339961	19990809
	AU 9956202	A1	20000306	AU 1999-56202	19990809
	BR 9912938	A	20010508	BR 1999-12938	19990809
	EP 1107964	A1	20010620	EP 1999-942827	19990809
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002522535	T	20020723	JP 2000-564947	19990809
	US 2002010181	A1	20020124	US 2001-781036	20010209
	US 6608071	B2	20030819		
PRAI	CH 1998-1654	A	19980811		
	WO 1999-EP5781	W	19990809		

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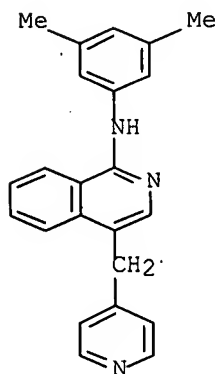
AB The title compds. [I;  $r = 0-2$ ;  $n = 0-2$ ;  $m = 0-4$ ; A, B, D, E = N, CH (with the proviso that not more than two of those radicals are N); G = alkylene, CH<sub>2</sub>O, CH<sub>2</sub>S, etc.; Q = alkyl, especially methyl; R = H, alkyl; X = NH, O, S; Y = alkyl, especially, aryl, heteroaryl, (un)substituted cycloalkyl; Z = (un)substituted NH<sub>2</sub>, halo, alkyl, etc.; the bonds indicated by a wavy line are either single bonds or double bonds] which inhibit especially angiogenesis, were prepared and formulated. E.g., a multi-step synthesis of II which showed IC<sub>50</sub> of 0.802  $\mu$ M against Flt-1 VEGF receptor tyrosine kinase, was given.

IT 258850-90-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of isoquinolines with angiogenesis inhibiting activity)

RN 258850-90-7 CAPLUS

CN 1-Isoquinolinamine, N-(3,5-dimethylphenyl)-4-(4-pyridinylmethyl)- (9CI)  
(CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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STN INTERNATIONAL LOGOFF AT 10:44:30 ON 23 AUG 2007